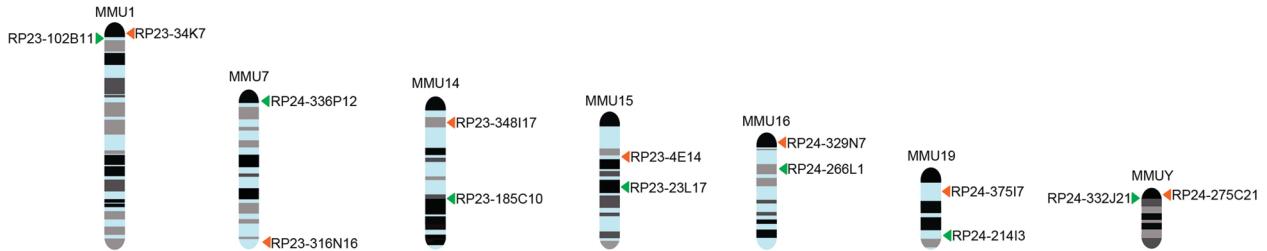
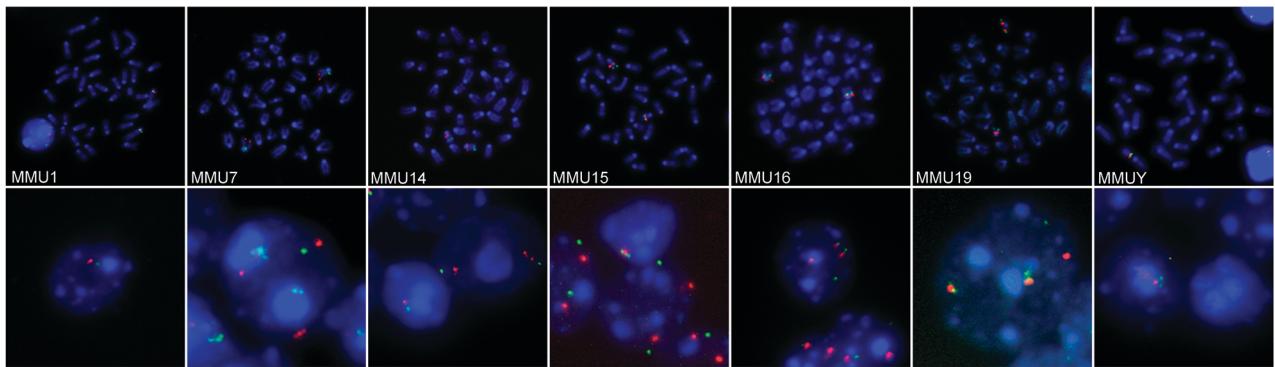


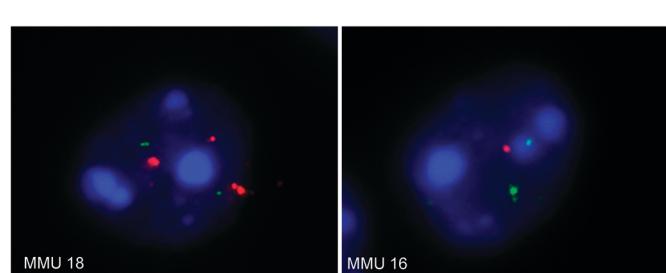
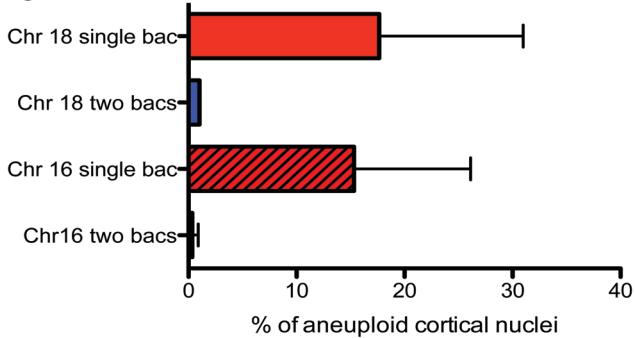
A



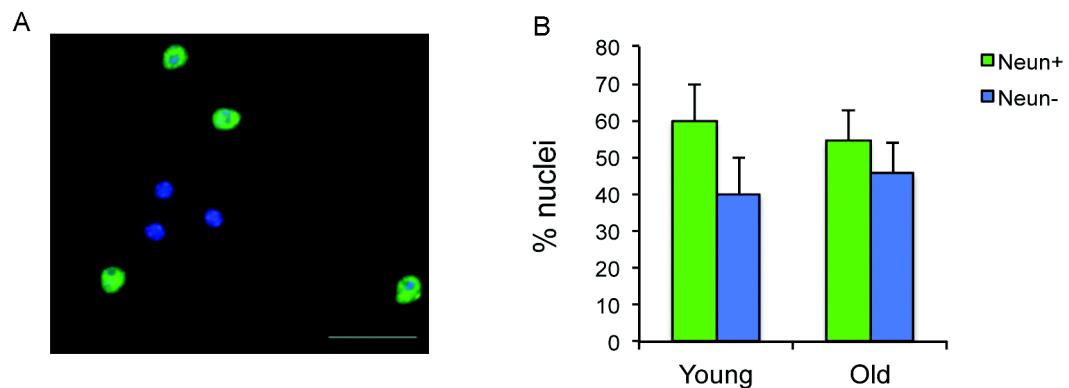
B



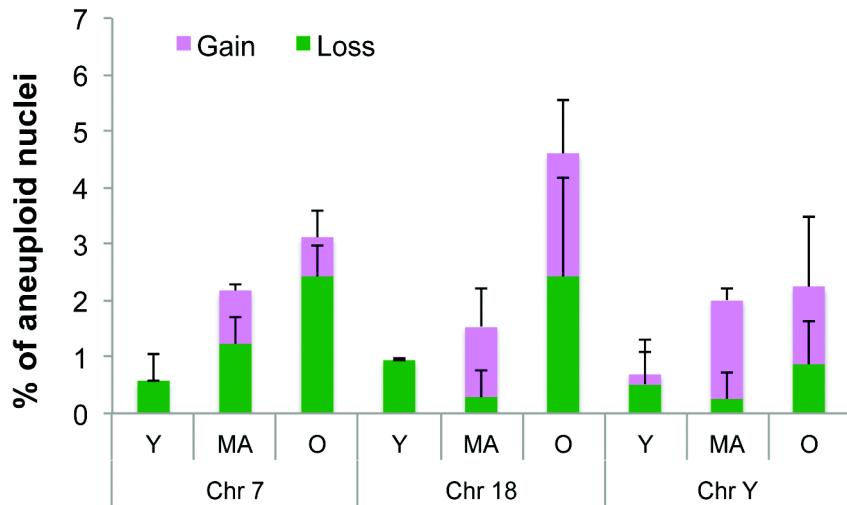
C



**Supplementary Figure 1.** (A). Probe design for FISH analysis. Mapping of the two target loci for each chromosome that were analyzed and identification of the respective BAC clones used in this study. (B). Top panel, examples of probe validation carried out using metaphase chromosomes obtained from splenocytes. Bottom panel, examples of aneuploid cortical nuclei corresponding to the chromosomes listed in the top panel. (C). Left panel, comparison between two different FISH approaches performed on three young (4- month C57BL/6) mice when analyzed for chromosomes 16 and 18 ( $n=100$  nuclei scored for each sample). Bars in red depict single locus specific probe and bars in blue two locus specific probes differently labeled. The use of the 2-colors FISH approach reduce sample to sample variation. Right panel, examples of hybridization for chromosome 18 and 16 showing the benefit of a two color approach.



**Supplementary Figure 2. (A)**. Percentage of NeuN+ cells in nuclei extracts. The heterogeneity of cortical samples was assessed by immunostaining with an antiNeuN antibody. Positive (neurons) are shown in green and negative (glia) are stained only with DAPI (blue). Bar 400mm. **(B)**. Summary of the percentage of neuronal (NeuN+) and non-neuronal (NeuN-) nuclei. The average for all young and old cortices analyzed is shown.



**Supplementary Figure 3.** Aneuploidy for chromosomes 7, Y and 18 is the result of balanced percentages of gains (green) and losses (pink). A trend towards loss is detected only for chromosome 7 and occurs across the three age groups.

Y=Young, MA=Middle Age, O=Old.

**Supplementary Table 1.** Cortical nuclei analyzed by FISH

		Total inspected nuclei for single chromosome										
Mice	Total inspected nuclei	Chr 1	Chr 7	Chr 14	Chr 15	Chr 16	Chr 18	Chr 19	Chr Y	Rate (%)	95% CI	
Y1	623	105	/	103	/	96	102	93	114	1.3	0.4 - 2.2	
Y2	505	96	/	105	/	105	107	92		1.6	0.5 - 2.7	
Y3	676	105	/	94	/	115	112	115	135	0.7	0.1 - 1.4	
Y4	886	106	116	97	111	123	112	110	111	0.7	0.1 - 1.2	
Y5	427	/	110	/	100	/	102	/	115	1.2	0.2 - 2.2	
Y6	472	/	124	/	123	/	109	/	116	0.6	0 - 1.4	
MA1	353	/	117	/	/	/	118	/	118	1.7	0.4 - 3.0	
MA2	332	/	93	/	/	/	111	/	128	1.8	0.4 - 3.2	
MA3	313	/	113	/	/	/	99	/	101	2.2	0.6 - 3.9	
O1	628	99	/	105	/	105	96	100	123	2.9	1.6 - 4.2	
O2	636	117	/	93	/	103	102	110	111	2.7	1.4 - 3.9	
O3	659	107	/	112	/	110	111	109	110	1.8	0.8 - 2.8	
O4	883	110	118	103	99	114	111	105	123	1.7	0.8 - 2.6	
O5	636	106	/	108	/	112	99	97	114	2.2	1.1 - 3.3	
O6	460	/	106	/	117	/	114	/	123	3.5	1.8 - 5.2	
O7	450	/	129	/	100	/	112	/	109	2.2	0.9 - 3.6	
O8	437	/	105	/	103	/	118	/	111	1.8	0.6 - 3.1	
<b>Total scored nuclei</b>	<b>9376</b>	<b>951</b>	<b>1131</b>	<b>920</b>	<b>753</b>	<b>983</b>	<b>1835</b>	<b>931</b>	<b>1862</b>			

**Supplementary Table 2.** FACS enriched NeuN+ and NeuN- cortical nuclei scored by FISH analysis

		Total inspected nuclei for single chromosome							
		Chr 1		Chr 18		NeuN+		NeuN-	
Mice	Total inspected nuclei	NeuN+	NeuN-	NeuN+	NeuN-	Rate (%)	95% CI	Rate (%)	95% CI
O1	404	100	98	106	100	0.015	0- 3.1	0.066	3.1-10.0
O2	413	98	103	102	110	0.036	1.0- 6.2	0.065	3.0-10.1
O3	380	100	96	96	88	0.005	0- 1.5	0.065	3.2-9.9
<b>Total scored nuclei</b>	<b>1197</b>	<b>298</b>	<b>297</b>	<b>304</b>	<b>288</b>				

**Supplementary Table 3.** Cerebellum nuclei analyzed by FISH

		Total inspected nuclei for single chromosome				
Mice	Total inspected nuclei	Chr 1	Chr 7	Chr 18	Rate (%)	95% CI
Y1	338	106	120	112	0.3	0 - 0.9
Y2	339	114	112	113	0.9	0 - 1.9
Y5	305	107	100	98	0.0	N.A.
O1	324	106	100	118	0.3	0- 0.9
O2	348	115	108	125	1.1	0- 2.3
O5	348	126	107	115	0.6	0-1.4
<b>Total scored nuclei</b>	<b>2002</b>	<b>674</b>	<b>647</b>	<b>681</b>		